REMARKS

Applicants respectfully requests entry of the remarks submitted herein. Claims 22-24, 27-29, 31-35, 38-43 are currently pending.

Rejection under 35 U.S.C. § 112, First Paragraph (Written Description)

The Examiner rejected claims 22-24, 27-36 and 38-43 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claims 30 and 36 were previously cancelled; therefore, Applicant will not address the rejection as applied to these claims.

Independent claim 22 recites a method to modulate vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction, comprising administering to the male patient a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof. Claims 23, 24, 27-29 and 31-32 depend either directly or indirectly from claim 22.

Independent claim 33 recites a method to modulate penile vascular tone in a male mammal in need thereof, said method comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof. Claims 34-35 and 38-42 depend either directly or indirectly from claim 33.

Independent claim 43 recites a method for treating erectile dysfunction in a male patient comprising administering to the male patient a composition comprising a CLC3 channel blocking agent or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The Office Action on page 3 states that "the terms 'male patient' is not specifically disclosed in the definition of specification as originally filed," and indicates that this is a "new matter" rejection. The Examiner is correct that the instant specification on page 21, lines 13-14, defines the term "patient" as "any living organism with vascular smooth muscle, such as a mammal, and, in particular, a human." It should be noted, however, that the term "patient" as recited in claim 22, is also limited by the adjectival phrase as "having compromised vascular tissue associated with erectile dysfunction" in addition to the adjective "male." Applicant respectfully submits that one of ordinary skill in the art would recognize that if the patient has

"compromised vascular tissue associated with erectile dysfunction" as recited in claim 22, then, logically, the patient is a male. Further, the specification from page 1, line 18 through page 6, line 22 sets forth the problem of male sexual dysfunction. Applicant therefore asserts that the term "male patient" is adequately described in the specification. Applicant respectfully requests that the Examiner withdraw the rejection of claims 22-24, 27-35, and 38-43 under 35 U.S.C. § 112, first paragraph (new matter).

The Office Action at page 3 states that "[t]he remaining claims are rejected to the extent that they depend on claim 22." As indicated above, claims 33-35, and 38-43 do not depend from claim 22. Therefore, Applicant requests that this rejection under 35 U.S.C. § 112, first paragraph, as applied to claims 33-35, and 38-43 be withdrawn.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 22-24, 27-29, 33-35 and 39-43 under 35 U.S.C. § 102(b) as being anticipated by Delaney *et al.* (1996) evidenced by Kifor *et al.* (US Patent No. 5,658,936), both of record. Applicant asserts that Delaney *et al.* fails to anticipate the present claims.

As discussed above, claims 22-24, 27-29, and 31-32 relate to methods for using a chloride channel blocking agent to modulate vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction. Claims 33-35 and 39-42 relate to methods for using a chloride channel blocking agent to modulate penile vascular tone in a male mammal in need thereof. Claim 43 recites a method for treating erectile dysfunction in a male patient. Applicant respectfully asserts that the present claims are not anticipated by Delaney *et al.*

Applicant respectfully submits that Delaney *et al.* does not teach the claimed methods. The Examiner states on page 3 of the Office Action that "the patient being treated by Delaney *et al.* had **enhanced** libido upon administration of tamoxifen" (emphasis in original), but then later states that "when tamoxifen treatment was continued, the libido condition was returned to normal." These two statements appear inconsistent to Applicant. It is unclear whether the Examiner believes that the tamoxifen treatment was the causative agent to increase the patient's libido, or if the tamoxifen treatment caused the patient's libido to reduce back down to a normal level. The Delaney *et al.* article states that the increased libido was a negative complication of

the tamoxifen treatment, as indicated by the statement that the patient "complained of two side-effects since the commencement of tamoxifen – the development of an acneform rash and for the immediately preceding 6 months significantly enhanced libido" (page 53, first column). There is no support in Delaney *et al.* for the examiner's statement on page 5 of the Office Action that "Delaney et al. continued tamoxifen in the patient while the patient was suffering from enhanced libido, to decrease the enhanced libido condition in the patient back to normal" (emphasis added).

Applicant asserts that Delaney *et al.* do not show a correlation between the administration of tamoxifen to the patient and the observed increase in libido in the patient. As discussed previously, the Delaney *et al.* reference discusses a case history of one male patient with metastatic breast cancer. The sequence of events was as follows:

Date	**Activity**
October 1988	Surgery for carcinoma
June 1992	Multiple bone metastases
February 1993	Radiotherapy
April 1993	Tamoxifen treatment started
August 1993	Side-effects began (significantly enhanced libido, rash)
February 1994	Patient seen for review, reported side-effects
January 1995	Patient re-evaluated, reported cessation of side-effects even though continued tamoxifen treatment (libido returned to normal, rash resolved)

Thus, during the middle portion of the period when he was treated with tamoxifen, he experienced increased libido. According to Delaney *et al.*, the patient began tamoxifen treatment in April of 1993. Ten months later, in February of 1994, he reported that he had experienced significantly enhanced libido for the immediately preceding six months. It is important to note that the onset of increased libido did not occur until the patient had been taking tamoxifen for about four months. Moreover, when the patient was reevaluated in January of 1995, his libido had returned to normal levels (and the other negative side effect of the rash resolved) despite the fact that he continued tamoxifen treatment. In other words, the patient's increased libido was not observed until the patient had been on tamoxifen for a several months, and it resolved before the patient discontinued his tamoxifen treatment.

Applicant asserts that there is a lack of causation (*i.e.*, a cause-and-effect relation) between the administration of tamoxifen and the effect observed by Delaney *et al.* Applicant

asserts that Delaney *et al.* do not show a correlation between the administration of tamoxifen to the patient and the observed increase in libido in the patient. The patient's increased libido was not observed until the patient had been on tamoxifen for a several months, and it resolved before the patient discontinued his tamoxifen treatment. Thus, Delaney *et al.* merely discloses that one male breast cancer patient on a tamoxifen regimen had experienced an increased libido during the course of treatment, and that the period of time in which he had an increased libido was not co-extensive with the period of time in which he was administered tamoxifen.

In summary, Delaney *et al.* do not anticipate claims 22-24 and 27-29, because Delaney *et al.* do not teach or suggest methods for using a chloride channel blocking agent to modulate vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction, as recited by claims 22-24 and 27-29. Instead, Delaney *et al.* teach treating a male breast cancer patient with tamoxifen. Delaney *et al.* do not anticipate claims 33-35 and 39-42, because Delaney do not teach or suggest methods for using a chloride channel blocking agent to modulate penile vascular tone in a mammal in need thereof. Delaney *et al.* do not discuss modulating penile vascular tone at all. Delaney *et al.* do not anticipate claim 43, because Delaney *et al.* do not teach or suggest a method for treating erectile dysfunction. They do not disclose any evidence that tamoxifen treatment and the observed increased libido were causatively linked.

Thus, Applicant asserts that the pending claims are not anticipated by Delaney *et al.*, and respectfully requests that the Examiner withdraw the rejection of claims 22-24, 27-29, 33-35, and 39-43 under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 31, 32, and 38 under 35 U.S.C. § 103(a) as being unpatentable over Delaney *et al.* (1996) and in further in view of Zhang *et al.* (U.S. Patent No. 6,266,560) and Drug Facts and Comparisons, 1997, all of record.

The Examiner stated that while Delaney *et al.* does not expressly teach the route of administration set forth in claims 32 and 38, or the further administration of the agents set forth in claim 31, that Drug Facts and Comparisons teaches that tamoxifen is commercially available in oral form, and that the Zhang *et al.* patent reports that vasodilators are useful for treatment of erectile dysfunction. Thus, the Examiner concluded that it would have been obvious to a

person having ordinary skill in the art to administer tamoxifen orally. The Examiner also concluded that it would have been obvious to incorporate a vasodilator agent with tamoxifen because vasodilators are useful for treatment of erectile dysfunction.

Claims 31 and 32 depend from claim 22 (which relates to methods for using a chloride channel blocking agent to modulate vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction), and claim 38 depends from claim 33 (which relates to methods to modulate penile vascular tone in a mammal in need thereof). As discussed above, Delaney *et al.* discloses only that one male patient experienced increased libido during a portion of the time for which he was on a tamoxifen regimen for the treatment of metastatic breast cancer. Delaney *et* al. do not establish causation for the patient's increased libido. At no point does the Delaney *et al.* reference teach or suggest a method of modulating vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction, or a method of modulating penile vascular tone.

The Zhang *et al.* patent and the Drug Facts and Comparisons document fail to remedy the deficiencies of Delaney *et al.* Neither of these documents suggest that a chloride channel blocking agent such as tamoxifen would be useful either to modulate vascular tone in a male patient having compromised vascular tissue associated with erectile dysfunction or to modulate penile vascular tone in a mammal in need thereof. Moreover, the combination of the Delaney *et al.* case study with the Zhang *et al.* patent and the Drug Facts and Comparisons document do not suggest that a chloride channel blocker would be useful to modulate vascular tone either alone or in combination with another agent (*e.g.*, a vasodilator), regardless of how it was administered. Thus, the combination of these three documents does not render claims 31, 32, and 38 obvious.

In light of the above, Applicant respectfully requests reversal of the Examiner's rejection of claims 31, 32, and 38 under 35 U.S.C. § 103(a).

CONCLUSION

The Examiner is invited to contact Applicant's Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.

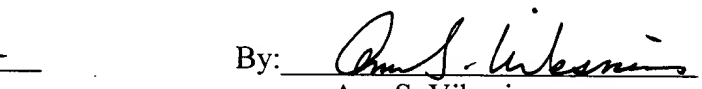
Respectfully submitted,

Fred S. Lamb et al.

By their Representatives,

Viksnins Harris & Padys PLLP
Customer Number 53137
PO Box 111098
St. Paul, MN 55111-1098
(952) 876-4091

Date: March 12, 2007

By: 
Ann S. Viksnins
Reg. No. 37,748